REMARKS

The Official Action dated April 4, 2006 has been carefully considered. Accordingly, the Amendment, taken with the following remarks, is believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By present amendment, independent claims 1, 13 and 14 have been amended, without prejudice as to the patentability of a broader scope, to limit the peptides to the specific peptides disclosed in the specification as efficacious for employment in the present methods at, for example, pages 7 and 8 and pages 15-21. The independent claims, along with dependent claims 4, 19 and 64, have been amended to insert or substitute the phrase "substantially corresponding," which is the phrase used in the specification to describe the contemplated scope. New claim 67 has been added and is explicitly supported by the instant specification at, for example, page 21, line 19 (using this phrase in relation to the specific peptides), and at page 14, lines 9-14 (defining homologue and analogue), and at page 21, line 21 bridging to page 22, lines 1-3 (discussing derivatives). The substance of these amendments comports with the Examiner's prior stated opinion as to sufficiency for compliance with the statutory mandates of 35 U.S.C. §112, and, further, do no involve the addition of new matter. Hence, it is believed that these amendments meet the description of suitable 1.116 amendments, and entry is therefore respectfully requested.

Claims 1, 4-14, 19 and 64-67 are pending and subject to examination.

35 U.S.C. § 112, first paragraph, "written description"

Claims 1, 4-14, 19 and 64 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that claims 1, 4-14, 19 and 64 encompass subject matter that is not defined in the specification. According to the Examiner, the claims are drawn to a method for inhibiting lipid oxidation associated with a condition in a patient, comprising administering to a patient a composition comprising a pharmacologically effective amount of an apolipoprotein (apo) A-IV peptide, to inhibit lipid oxidation, and that "the claimed invention asserts that the apo A-IV is a peptide sequence of from 6-71 amino acids in length and wherein the peptide has substantially the same lipid oxidation properties as the apo A-IV molecule. The Examiner notes the present teachings at page 6 discussing the peptides made from apo A-I, their properties, and their efficacy in treating atherosclerosis, but asserts that the specification does not describe the specific structure and function of these sequence fragments. The Examiner further asserts that the limitation of 6-71 amino acids in length fails to define whether the sequence is derived from native apo A-IV, and that a sequence identifier has not been given to this sequence. The Examiner points to the present teachings that the lipid oxidation inhibiting peptides substantially correspond in sequence to amino acid sequences found in specific portions of apo A-IV, and asserts that this is an insufficient description since there are no characteristics or evidence provided to demonstrate retention of function with regard to inhibitory activity in lipid oxidation.

With respect particularly to claim 4, the Examiner asserts that the specification only "provides a generic description of how a variety of variants or fragments can be generated, and that no specific guidance is provided on generation of variants or fragments that demonstrate biological activity of the peptide sequence of SEQ ID NO 5." Broadly, the Examiner maintains that the Applicants are "not in possession of the apo A-IV, which

comprises variants and fragments, which have substantially the same lipid oxidation properties as the apo A-IV wild-type molecule," and that there is no written description of either a representative number of the variants or of a common structural feature of the native apo A-IV that encompasses all the variants.

Summarily, the Examiner asserts that one of ordinary skill in the art "would not recognize from the disclosure that Applicants were in possession of the apo A-IV, which comprises variants and fragments, which have substantially the same lipid oxidation properties as the apo A-IV wild type molecule," and that "there is no written description of either a representative number of the variants or of a common structural feature of the native apo A-IV that encompasses all the variants." This rejection is traversed and reconsideration is respectfully requested

The independent claims have all been amended to specifically recite, inter alia, that the apolipoprotein A-IV peptide employed in the presently inventive methods comprises an amino acid sequence substantially corresponding to at least one of the sequences set forth as: SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO: 4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; and SEQ ID NO:13.

Specifically, independent claim 1 recites a method for inhibiting lipid oxidation associated with a condition in a patient. The method comprises administering to a patient a composition comprising a pharmacologically effective amount of an apolipoprotein (apo) A-IV peptide to inhibit lipid oxidation. The apolipoprotein A-IV peptide is from 6 to 71 amino acids in length and comprises a sequence as noted above. Further, the peptide has substantially the same lipid oxidation properties as the apolipoprotein A-IV molecule.

Independent claim 13 recites a method of inhibiting the progression of atherosclerosis in a patient in need thereof. The method comprises administering to the patient a composition comprising an effective anti-oxidation amount of an apolipoprotein (apo) A-IV to inhibit the progression of atherosclerosis. The apolipoprotein A-IV peptide is from 6 to 71 amino acids in length and comprises a sequence as noted above, and has substantially the same lipid oxidation properties as the apolipoprotein A-IV molecule.

Independent claim 14 is directed to a method of treating a patient for atherosclerosis. The method comprises administering to the patient a composition comprising an effective anti-oxidation amount of an apolipoprotein (apo) A-IV peptide. The apolipoprotein A-IV peptide is from 6 to 71 amino acids in length and comprises a sequence as noted above. The peptide has substantially the same lipid oxidation properties as the apolipoprotein A-IV molecule.

Written support for the specifically recited peptides no longer relies on the structure or function arguments rejected by the Examiner. While Applicants believe that these specifically disclosed and recited peptides are sufficiently representative of the broader genus, for purposes of expediting prosecution Applicants have limited the independent claims to the peptides specifically disclosed, without prejudice as to the patentability of a claim having broader scope. The inventive peptides set forth in the independent claims are specifically disclosed in the present specification at pages 7-8, and pages 15-21 as examples of preferred peptides (page 15, line 21, e.g.).

With respect in particular to claim 4, Applicants are confused by the Examiner's reference to "fragments." Applicants note that this term was already removed from the claim in response to a request by the Examiner for an Examiner's amendment in 2005. Claim 4 is

directed to a specific species of the inventive peptide that is expressly supported by the specification, including by a precise statement of the sequence and submission of this sequence in a requisite Sequence Listing. The term "substantially corresponds" is used throughout the present specification and is expressly defined (e.g. page 22, lines 19-21)) as an amino acid sequence having approximately 70% homology to a specifically recited amino acid sequence.

As support for the subject matter of independent claims 1, 13 and 14 no longer relies on structure or function based arguments that involve subjective notions of "representative" or "similar," but, rather, relies on express objective disclosure of the specifically recited species, Applicants submit that these claims, and claims dependent therefrom, are fully supported by the written description in the specification. Hence, the rejection of claims 1, 4-14, 19 and 64-66 under 35 U.S.C. §112, first paragraph, has been overcome. Reconsideration is therefore respectfully requested.

35 U.S.C. § 112, first paragraph "enablement"

Claims 1, 4-14, 19 and 64-66 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification, while being enabling for a method for inhibiting lipid oxidation associated with a condition in a patient comprising administering an apo A-IV compound, does not reasonably provide enablement for a method of inhibiting lipid oxidation comprising administering "all apo A-IV variants/fragments," such that the specification does not enable persons skilled in the art to make and/or use the invention commensurate in scope with the claims, without undue experimentaion. Specifically, the Examiner lists 8 factors considered in an analysis determining whether undue experimentation is required to practice the invention. In particular, the Examiner asserts that "the specification needs to provide

specific guidance on the treating conditions such as the dosage, the time and effect for treating conditions associated with lipid oxidation for various apo A-IV protein products, to be considered enabling for variants." This rejection is traversed and reconsideration is respectfully requested.

Applicants appreciate the Examiner's acknowledgement that the present disclosure is "enabling for a method for inhibiting lipid oxidation associated with a condition in a patient comprising administering an apo A-IV compound." Applicants note that the present amendment to the independent claims, as set forth in detail above, addresses the Examiner's concern that methods involving administration of all apo A-IV "variants/fragments" are not similarly enabled. Independent claims 1, 13 and 14 recite specific apo A-IV peptides and practice of the inventive methods by employment of these peptides does not require an inventive step or undue experimentation on the part of the ordinary practitioner. The specification provides ample guidance on the synthesis of these peptides and further notes that these peptides, derived from apo A-IV, retain efficacy with respect to inhibition of lipid oxidation. An ordinary practitioner merely needs to apply knowledge readily available in the art to employ the presently disclosed peptides in the presently disclosed methods in order to achieve the desired benefit.

Applicants believe that the present specification provides sufficient guidance to an ordinary practitioner in the art as to the synthesis of peptides expected to exhibit efficacy in the invented methods. However, for purposes of expediting prosecution of the application, Applicants have limited the inventive methods to employment of the specifically disclosed peptides, without prejudice as to the patentability of claims directed to broader embodiments.

Applicants appreciate the Examiner's acknowledgment that enablement under § 112, paragraph one, in the case of pharmaceutical arts, does not require disclosure of clinical parameters or working examples of drug administration. Applicants further appreciate the clarification, on page 8 of the April 6 Office Action, that the rejection is based on an asserted lack of guidance with respect to employment of "fragments or variants" in the inventive methods. As noted, however, the present specification discloses dosage guidance on paged 26 and 31 of the present specification (page 26, first and second full paragraphs, page 31, last paragraph). Detailed administration guidelines and formulation guidelines are provided on pages 26-31. Admittedly, comporting with common PTO practice and due in part to the nature of the therapeutic arts, Applicants disclose this information with the caveat that such end uses must be determined according to specific concerns of the patient and practitioner. Under the pretext of this caveat, however, guidelines for the manufacture of pharmaceutical compositions and products are also provided, for example, on page 33.

With respect to "working examples," Applicants disclose treatment regimens, dosages, suggested routes of administration, and other matters of clinical concern, taking into consideration the nature of the conditions disclosed as treatable by these actives, and the properties of the actives themselves. Applicants submit that it is well within the ability of a person of ordinary skill in the medicinal and therapeutic arts to determine optimum dosages, suitable composition excipients and additives, suitable forms for administration, and the like, by routine experimentation and knowledge common to the art.

The enablement requirement of §112, first paragraph, as judicially interpreted by case law, requires that the specification must provide sufficient teaching such that one skilled in the art could make and use the full scope of the invention without undue experimentation.

CFMT, Inc. v. Yieldup Int'l Corp., 68 USPQ2d 1940, 1944 (Fed. Cir. 2003); *In re Wands*, 8 USPQ2d 1400, 1405 (Fed. Cir. 1988). "The key word is 'undue,' not experimentation.'" *Wands*, 8 USPQ2d at 1405 (citation omitted). That is, the specification need only teach those aspects of the invention that one skilled in the art could not discern without undue experimentation. *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 49 USPQ2d 1671, 1673 (Fed. Cir. 1999) ("The scope of enablement ...is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation"); *Wands*, 8 USPQ2d at 1404-1405 ("Enablement is not precluded by the necessity for some experimentation such as routine screening.").

Applicants submit that it is within the ability of a person of ordinary skill in the protein arts to employ the presently recited apo A-IV peptides in the inventive methods to achieve the desired benefit as stated in the present specification and as supported by the examples and data disclosed therein.

Hence, the rejection of claims 1, 4-14, 19 and 64-66, under 35 U.S.C. §112, first paragraph, for lack of enablement by the specification has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Examiner's rejection of the claims under 35 U.S.C. §§112, first paragraph, "written description" and "enablement" clauses, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,

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